SEQUENCE LISTING

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<110> Yan et al.
<120> SUBSTRATES AND ASSAYS FOR BETA-SECRETASE ACTIVITY
<130> 29915/00281C
<140> To be assigned
<141> 2004-03-16
<150> 09/908,943
<151> 2001-07-19
<150> 60/219,795
<151> 2000-07-19
<160> 197
<170> PatentIn Ver. 2.0
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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser 20 25 30

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Glu Glu Pro Glu Glu Pro Gly Arg Gly Ser Phe Val Glu Met Val
50 55 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 145 150 155 . 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp 180 185 190

Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro 195 200 205

Asn Leu Phe Ser Leu His Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln 210 215 220

Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile 225 230 235 240

Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg 245 : 250 255

Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln 260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val 275 280 285

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Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
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Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
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Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
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Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
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Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
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Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
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Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu
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peptide sequence

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Lys
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Phe Phe Ala Glu
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Leu Val Xaa Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Ala
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Glu Asn Tyr Xaa Asn
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Tyr Arg Tyr Gln Ser His Asp Tyr Ala Phe Ser Ser Val Glu Lys Leu
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Leu His Ala Leu Gly Gly Cys
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<400> 38
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peptide sequence
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Xaa Ala Asn Tyr Glu Val Glu Phe
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<210> 51
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<222> (3)
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Glu Ala Xaa Tyr Glu Val Glu Phe
        5
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<223> Xaa= any amino acid
<220>
<221> SITE
<222> (4)..(7)
<223> Xaa= any amino acid
<220>
<221> SITE
<222> (8)
<223> Xaa= F, W, G, A, H, P, G, N or S
<400> 112
Xaa Phe Ala Xaa Xaa Xaa Xaa
 1
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<210> 113
<211> 9
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 113
Glu Val Asn Leu Asp Ala Glu Phe Arg
<210> 114
<211> 7
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 114
Asp Tyr Lys Asp Asp Asp Lys
<210> 115
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 115
Ala Cys Gly Ser Glu Ser Met Asp Ser Gly Ile Ser Leu Asp Asn Lys
Trp
<210> 116
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 116
Trp Lys Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Lys
Lys
```

```
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 117
Ala Asn Leu Ser Thr Phe Ala Gln Pro Arg Arg
 1
                  5
                                      10
<210> 118
<211> 22
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 118
Tyr Arg Tyr Gln Ser His Asp Tyr Ala Phe Ser Ser Val Glu Lys Leu
                                      10
Leu His Leu Gly Gly Cys
             20
<210> 119
<211> 22
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 119
Tyr Arg Tyr Gln Ser His Asp Tyr Ala Phe Ser Ser Val Glu Lys Leu
                                      10
Leu His Leu Gly Gly Cys
             20
<210> 120
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 120
Lys Thr Ile Thr Leu Glu Val Glu Pro Ser
                 5
                                      10
<210> 121
<211> 12
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<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<220>
<221> SITE
<222> (9)
<223> Xaa= cysteic acid
<400> 121
Val Glu Ala Leu Tyr Leu Val Cys Xaa Gly Glu Arg
                 5
<210> 122
<211> 11
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 122 .
Val Glu Ala Leu Tyr Leu Val Glu Gly Glu Arg
<210> 123
<211> 363
<212> PRT
<213> Homo sapiens
<220>
<223> galactosyltransferase
Met Ala Ser Lys Ser Trp Leu Asn Phe Leu Thr Phe Leu Cys Gly Ser
Ala Ile Gly Phe Leu Leu Cys Ser Gln Leu Phe Ser Ile Leu Leu Gly
             20
Glu Lys Val Asp Thr Gln Pro Asn Val Leu His Asn Asp Pro His Ala
Arg His Ser Asp Asp Asn Gly Gln Asn His Leu Glu Gly Gln Met Asn
Phe Asn Ala Asp Ser Ser Gln His Lys Asp Glu Asn Thr Asp Ile Ala
                                         75
Glu Asn Leu Tyr Gln Lys Val Arg Ile Leu Cys Trp Val Met Thr Gly
Pro Gln Asn Leu Glu Lys Lys Ala Lys His Val Lys Ala Thr Trp Ala
Gln Arg Cys Asn Lys Val Leu Phe Met Ser Ser Glu Glu Asn Lys Asp
        115
                            120
                                                 125
```

Phe Pro Ala Val Gly Leu Lys Thr Lys Glu Gly Arg Asp Gln Leu Tyr 130 140

Trp Lys Thr Ile Lys Ala Phe Gln Tyr Val His Glu His Tyr Leu Glu

Asp Ala Asp Trp Phe Leu Lys Ala Asp Asp Asp Thr Tyr Val Ile Leu 165 170 175

Asp Asn Leu Arg Trp Leu Leu Ser Lys Tyr Asp Pro Glu Glu Pro Ile 180 185 190

Tyr Phe Gly Arg Arg Phe Lys Pro Tyr Val Lys Gln Gly Tyr Met Ser 195 200 205

Gly Gly Ala Gly Tyr Val Leu Ser Lys Glu Ala Leu Lys Arg Phe Val 210 215 220

Asp Ala Phe Lys Thr Asp Lys Cys Thr His Ser Ser Ser Ile Glu Asp 225 230 235 240

Leu Ala Leu Gly Arg Cys Met Glu Ile Met Asn Val Glu Ala Gly Asp 245 250 255

Ser Arg Asp Thr Ile Gly Lys Glu Thr Phe His Pro Phe Val Pro Glu 260 265 270

His His Leu Ile Lys Gly Tyr Leu Pro Arg Thr Phe Trp Tyr Trp Asn 275 280 285

Tyr Asn Tyr Tyr Pro Pro Val Glu Gly Pro Gly Cys Cys Ser Asp Leu 290 295 300

Ala Val Ser Phe His Tyr Val Asp Ser Thr Thr Met Tyr Glu Leu Glu 305 310 315 320

Tyr Leu Val Tyr His Leu Arg Pro Tyr Gly Tyr Leu Tyr Arg Tyr Gln 325 330 335

Pro Thr Leu Pro Glu Arg Ile Leu Lys Glu Ile Ser Gln Ala Asn Lys 340 345 350

Asn Glu Asp Thr Lys Val Lys Leu Gly Asn Pro 355 360

<210> 124

<211> 405

<212> PRT

<213> Homo sapiens

<220>

<223> Homo sapiens sialylytransferase 1

<400> 124

Ile His Thr Asn Leu Lys Lys Phe Ser Cys Cys Val Leu Val Phe
1 5 10 15

Leu Leu Phe Ala Val Ile Cys Val Trp Lys Glu Lys Lys Gly Ser 20 25 30

Tyr Tyr Asp Ser Phe Lys Leu Gln Thr Lys Glu Phe Gln Val Leu Lys

35 40 45

Ser Leu Gly Lys Leu Ala Met Gly Ser Asp Ser Gln Ser Val Ser Ser 55 Ser Ser Thr Gln Asp Pro His Arg Gly Arg Gln Thr Leu Gly Ser Leu Arg Gly Leu Ala Lys Ala Lys Pro Glu Ala Ser Phe Gln Val Trp Asn Lys Asp Ser Ser Ser Lys Asn Leu Ile Pro Arg Leu Gln Lys Ile Trp 105 Lys Asn Tyr Leu Ser Met Asn Lys Tyr Lys Val Ser Tyr Lys Gly Pro 120 Gly Pro Gly Ile Lys Phe Ser Ala Glu Ala Leu Arg Cys His Leu Arg Asp His Val Asn Val Ser Met Val Glu Val Thr Asp Phe Pro Phe Asn 155 Thr Ser Glu Trp Glu Gly Tyr Leu Pro Lys Glu Ser Ile Arg Thr Lys Ala Gly Pro Trp Gly Arg Cys Ala Val Val Ser Ser Ala Gly Ser Leu 180 Lys Ser Ser Gln Leu Gly Arg Glu Ile Asp Asp His Asp Ala Val Leu Arg Phe Asn Gly Ala Pro Thr Ala Asn Phe Gln Gln Asp Val Gly Thr Lys Thr Thr Ile Arg Leu Met Asn Ser Gln Leu Val Thr Thr Glu Lys 230 Arg Phe Leu Lys Asp Ser Leu Tyr Asn Glu Gly Ile Leu Ile Val Trp Asp Pro Ser Val Tyr His Ser Asp Ile Pro Lys Trp Tyr Gln Asn Pro Asp Tyr Asn Phe Phe Asn Asn Tyr Lys Thr Tyr Arg Lys Leu His Pro 280 Asn Gln Pro Phe Tyr Ile Leu Lys Pro Gln Met Pro Trp Glu Leu Trp Asp Ile Leu Gln Glu Ile Ser Pro. Glu Glu Ile Gln Pro Asn Pro Pro 315 Ser Ser Gly Met Leu Gly Ile Ile Ile Met Met Thr Leu Cys Asp Gln 325. 330 Val Asp Ile Tyr Glu Phe Leu Pro Ser Lys Arg Lys Thr Asp Val Cys Tyr Tyr Gln Lys Phe Phe Asp Ser Ala Cys Thr Met Gly Ala Tyr His Pro Leu Leu Tyr Glu Lys Asn Leu Val Lys His Leu Asn Gln Gly 370 375 380

Thr Asp Glu Asp Ile Tyr Leu Leu Gly Lys Ala Thr Leu Pro Gly Phe 385 390 395 400

Arg Thr Ile His Cys

<210> 125

<211> 518

<212> PRT

<213> Homo sapiens

<220>

<223> Homo sapiens aspartyl protease 1

<400> 125

Met Gly Ala Leu Ala Arg Ala Leu Leu Leu Pro Leu Leu Ala Gln Trp

1 10 15

Leu Leu Arg Ala Ala Pro Glu Leu Ala Pro Ala Pro Phe Thr Leu Pro
20 25 30

Leu Arg Val Ala Ala Ala Thr Asn Arg Val Val Ala Pro Thr Pro Gly
35 40 45

Pro Gly Thr Pro Ala Glu Arg His Ala Asp Gly Leu Ala Leu 50 55 60

Glu Pro Ala Leu Ala Ser Pro Ala Gly Ala Ala Asn Phe Leu Ala Met 65 70 75 80

Val Asp Asn Leu Gln Gly Asp Ser Gly Arg Gly Tyr Tyr Leu Glu Met 85 90 95

Leu Ile Gly Thr Pro Pro Gln Lys Leu Gln Ile Leu Val Asp Thr Gly
100 105 110

Ser Ser Asn Phe Ala Val Ala Gly Thr Pro His Ser Tyr Ile Asp Thr 115 120 125

Tyr Phe Asp Thr Glu Arg Ser Ser Thr Tyr Arg Ser Lys Gly Phe Asp 130 135 140

Val Thr Val Lys Tyr Thr Gln Gly Ser Trp Thr Gly Phe Val Gly Glu 145 150 155 160

Asp Leu Val Thr Ile Pro Lys Gly Phe Asn Thr Ser Phe Leu Val Asn 165 170 175

Ile Ala Thr Ile Phe Glu Ser Glu Asn Phe Phe Leu Pro Gly Ile Lys 180 185 190

Trp Asn Gly Ile Leu Gly Leu Ala Tyr Ala Thr Leu Ala Lys Pro Ser 195 200 205

Ser Ser Leu Glu Thr Phe Phe Asp Ser Leu Val Thr Gln Ala Asn Ile 210 215 220

Pro Asn Val Phe Ser Met Gln Met Cys Gly Ala Gly Leu Pro Val Ala 225 230 235 240 Gly Ser Gly Thr Asn Gly Gly Ser Leu Val Leu Gly Gly Ile Glu Pro 245 250 255

Ser Leu Tyr Lys Gly Asp Ile Trp Tyr Thr Pro Ile Lys Glu Glu Trp
260 265 270

Tyr Tyr Gln Ile Glu Ile Leu Lys Leu Glu Ile Gly Gly Gln Ser Leu
275 280 285

Asn Leu Asp Cys Arg Glu Tyr Asn Ala Asp Lys Ala Ile Val Asp Ser 290 295 300

Gly Thr Thr Leu Leu Arg Leu Pro Gln Lys Val Phe Asp Ala Val 305 310 315 320

Glu Ala Val Ala Arg Ala Ser Leu Ile Pro Glu Phe Ser Asp Gly Phe
325 330 335

Trp Thr Gly Ser Gln Leu Ala Cys Trp Thr Asn Ser Glu Thr Pro Trp 340 345 350

Ser Tyr Phe Pro Lys Ile Ser Ile Tyr Leu Arg Asp Glu Asn Ser Ser 355 360 365

Arg Ser Phe Arg Ile Thr Ile Leu Pro Gln Leu Tyr Ile Gln Pro Met 370 380

Met Gly Ala Gly Leu Asn Tyr Glu Cys Tyr Arg Phe Gly Ile Ser Pro 385 390 395 400

Ser Thr Asn Ala Leu Val Ile Gly Ala Thr Val Met Glu Gly Phe Tyr 405 410 415

Val Ile Phe Asp Arg Ala Gln Lys Arg Val Gly Phe Ala Ala Ser Pro 420 425 430

Cys Ala Glu Ile Ala Gly Ala Ala Val Ser Glu Ile Ser Gly Pro Phe 435 440 445

Ser Thr Glu Asp Val Ala Ser Asn Cys Val Pro Ala Gln Ser Leu Ser 450 455 460

Glu Pro Ile Leu Trp Ile Val Ser Tyr Ala Leu Met Ser Val Cys Gly 465 470 475 480

Ala Ile Leu Leu Val Leu Ile Val Leu Leu Leu Leu Pro Phe Arg Cys
485 490 495

Gln Arg Arg Pro Arg Asp Pro Glu Val Val Asn Asp Glu Ser Ser Leu 500 505 510

Val Arg His Arg Trp Lys 515

<210> 126

<211> 255

<212> PRT

<213> Homo sapiens

<220>

<223> Homo sapiens syntaxin 6

<400> 126

Met Ser Met Glu Asp Pro Phe Phe Val Val Lys Gly Glu Val Gln Lys 1 5 10 15

Ala Val Asn Thr Ala Gln Gly Leu Phe Gln Arg Trp Thr Glu Leu Leu 20 25 30

Gln Asp Pro Ser Thr Ala Thr Arg Glu Glu Ile Asp Trp Thr Thr Asn 35 40 45

Glu Leu Arg Asn Asn Leu Arg Ser Ile Glu Trp Asp Leu Glu Asp Leu 50 60

Asp Glu Thr Ile Ser Ile Val Glu Ala Asn Pro Arg Lys Phe Asn Leu 65 70 75 80

Asp Ala Thr Glu Leu Ser Ile Arg Lys Ala Phe Ile Thr Ser Thr Arg 85 90 95

Gln Val Val Arg Asp Met Lys Asp Gln Met Ser Thr Ser Ser Val Gln
100 105 110

Ala Leu Ala Glu Arg Lys Asn Arg Gln Ala Leu Leu Gly Asp Ser Gly 115 120 125

Ser Gln Asn Trp Ser Thr Gly Thr Thr Asp Lys Tyr Gly Arg Leu Asp 130 135 140

Arg Glu Leu Gln Arg Ala Asn Ser His Phe Ile Glu Glu Gln Gln Ala 145 150 155 160

Gln Gln Gln Leu Ile Val Glu Gln Gln Asp Glu Gln Leu Glu Leu Val 165 170 175

Ser Gly Ser Ile Gly Val Leu Lys Asn Met Ser Gln Arg Ile Gly Gly 180 185 190

Glu Leu Glu Glu Gln Ala Val Met Leu Glu Asp Phe Ser His Glu Leu 195 200 205

Glu Ser Thr Gln Ser Arg Leu Asp Asn Val Met Lys Lys Leu Ala Lys 210 220

Val Ser His Met Thr Ser Asp Arg Arg Gln Trp Cys Ala Ile Ala Ile 225 230 235 240

Leu Phe Ala Val Leu Leu Val Val Leu Ile Leu Phe Leu Val Leu 245 250 255

<210> 127

<211> 1728

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: nucleic acid encoding recombinant fusion protein

<400> 127

atgetgetge tgetgetget getgggeetg aggetaeage tetecetggg cateateeea 60 gttgaggagg agaaceegga ettetggaae egegaggeag eegaggeeet gggtgeegee 120 aagaagetge ageetgeaea gaeageegee aagaaeetea teatetteet gggegatggg 180

atgggggtgt ctacggtgac agctgccagg atcctaaaag ggcagaagaa ggacaaactg 240

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gggcctgaga tacccctggc catggaccgc ttcccatatg tggctctqtc caaqacatac 300
aatgtagaca aacatgtgcc agacagtgga gccacagcca cggcctacct gtgcggggtc 360
aagggcaact tccagaccat tggcttgagt gcagccgccc gctttaacca gtgcaacacg 420
acacgcggca acgaggtcat ctccgtgatg aatcgggcca agaaagcagg gaagtcagtg 480
ggagtggtaa ccaccacacg agtgcagcac gcctcqccaq ccqqcaccta cqcccacacq 540
gtgaaccgca actggtactc ggacgccgac gtgcctgcct cggcccgcca ggaggggtgc 600
caggacatcg ctacgcagct catctccaac atggacattg acgtgatcct aggtggaggc 660
cgaaagtaca tgtttcccat gggaacccca gaccctgagt acccagatga ctacagccaa 720
ggtgggacca ggctggacgg gaagaatctg gtgcaggaat ggctggcgaa gcgccagggt 780
gcccggtatg tgtggaaccg cactgagete atgcaggett ccctggacce gtctgtgacc 840
catctcatgg gtctctttga gcctggagac atgaaatacg agatccaccq agactccaca 900
ctggacccct ccctgatgga gatgacagag gctgccctgc gcctgctgag caggaacccc 960
cgcggcttct tcctcttcgt ggagggtggt cgcatcgacc atggtcatca tgaaagcagg 1020
gcttaccggg cactgactga gacgatcatg ttcgacgacg ccattgagag ggcgggccag 1080
ctcaccagcg aggaggacac gctgagcctc gtcactgccg accactccca cgtcttctcc 1140
ttcggagget acccettgeg agggagetee atetteggge tggeeeetgg caaggeeegg 1200
gacaggaagg cctacacggt cctcctatac ggaaacggtc caggctatgt gctcaaggac 1260
ggcgcccggc cggatgttac cgagagcgag agcgggagcc ccgagtatcg gcagcagtca 1320
gcagtgcccc tggacgaaga gacccacgca ggcgaggacg tggcggtgtt cgcgcgcggc 1380
ccgcaggcgc acctggttca cggcgtgcag gagcagacct tcatagcgca cgtcatggcc 1440
ttegeegeet geetggagee ctacacegee tgegacetgg egeeeeege eggcaceaee 1500
gacgccgcgc acccaggtaa ctatgaagtt gaattccgaa gagcactcta cgtagagggt 1560
gaaagaggat tettetacae tecaaaggea etetaceteg tagagggtga aagaggatte 1620
ttctacacta gtctcatgac catagcctat gtcatggctg ccatctgcgc cctcttcatg 1680
ctgccactct gcctcatggt ggactacaag gatgatgatg acaagtag
<210> 128
<211> 575
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: recombinant
      fusion protein sequence
<400> 128
Met Leu Leu Leu Leu Leu Leu Gly Leu Arg Leu Gln Leu Ser Leu
                                     10
Gly Ile Ile Pro Val Glu Glu Asn Pro Asp Phe Trp Asn Arg Glu
Ala Ala Glu Ala Leu Gly Ala Ala Lys Lys Leu Gln Pro Ala Gln Thr
Ala Ala Lys Asn Leu Ile Ile Phe Leu Gly Asp Gly Met Gly Val Ser
Thr Val Thr Ala Ala Arg Ile Leu Lys Gly Gln Lys Lys Asp Lys Leu
65
Gly Pro Glu Ile Pro Leu Ala Met Asp Arg Phe Pro Tyr Val Ala Leu
Ser Lys Thr Tyr Asn Val Asp Lys His Val Pro Asp Ser Gly Ala Thr
Ala Thr Ala Tyr Leu Cys Gly Val Lys Gly Asn Phe Gln Thr Ile Gly
Leu Ser Ala Ala Ala Arg Phe Asn Gln Cys Asn Thr Thr Arg Gly Asn
    130
                        135
                                            140
```

Glu Val Ile Ser Val Met Asn Arg Ala Lys Lys Ala Gly Lys Ser Val 150 Gly Val Val Thr Thr Arg Val Gln His Ala Ser Pro Ala Gly Thr 170 Tyr Ala His Thr Val Asn Arg Asn Trp Tyr Ser Asp Ala Asp Val Pro Ala Ser Ala Arg Gln Glu Gly Cys Gln Asp Ile Ala Thr Gln Leu Ile 200 Ser Asn Met Asp Ile Asp Val Ile Leu Gly Gly Gly Arg Lys Tyr Met Phe Pro Met Gly Thr Pro Asp Pro Glu Tyr Pro Asp Asp Tyr Ser Gln Gly Gly Thr Arg Leu Asp Gly Lys Asn Leu Val Gln Glu Trp Leu Ala 250 Lys Arg Gln Gly Ala Arg Tyr Val Trp Asn Arg Thr Glu Leu Met Gln Ala Ser Leu Asp Pro Ser Val Thr His Leu Met Gly Leu Phe Glu Pro Gly Asp Met Lys Tyr Glu Ile His Arg Asp Ser Thr Leu Asp Pro Ser 295 300 Leu Met Glu Met Thr Glu Ala Ala Leu Arg Leu Leu Ser Arg Asn Pro Arg Gly Phe Phe Leu Phe Val Glu Gly Gly Arg Ile Asp His Gly His 330 His Glu Ser Arg Ala Tyr Arg Ala Leu Thr Glu Thr Ile Met Phe Asp 345 Asp Ala Ile Glu Arg Ala Gly Gln Leu Thr Ser Glu Glu Asp Thr Leu Ser Leu Val Thr Ala Asp His Ser His Val Phe Ser Phe Gly Gly Tyr 370 375 380 Pro Leu Arg Gly Ser Ser Ile Phe Gly Leu Ala Pro Gly Lys Ala Arg Asp Arg Lys Ala Tyr Thr Val Leu Leu Tyr Gly Asn Gly Pro Gly Tyr Val Leu Lys Asp Gly Ala Arg Pro Asp Val Thr Glu Ser Glu Ser Gly 425 Ser Pro Glu Tyr Arg Gln Gln Ser Ala Val Pro Leu Asp Glu Glu Thr His Ala Gly Glu Asp Val Ala Val Phe Ala Arg Gly Pro Gln Ala His Leu Val His Gly Val Gln Glu Gln Thr Phe Ile Ala His Val Met Ala 470 475

```
Phe Ala Ala Cys Leu Glu Pro Tyr Thr Ala Cys Asp Leu Ala Pro Pro
                485
                                    490
Ala Gly Thr Thr Asp Ala Ala His Pro Gly Asn Tyr Glu Val Glu Pro
Arg Arg Ala Leu Tyr Val Glu Gly Glu Arg Gly Phe Phe Tyr Thr Pro
Lys Ala Leu Tyr Leu Val Glu Gly Glu Arg Gly Phe Phe Tyr Thr Ser
    530
Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met
Leu Pro Leu Cys Leu Met Val Asp Tyr Lys Asp Asp Asp Lys
                                    570
<210> 129
<211> 5
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 129
Lys Met Asp Ala Glu
<210> 130
<211> 5
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 130
Gly Arg Arg Gly Ser
 1
<210> 131
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 131
Val Glu Ala Asn Tyr Glu Val Glu Gly Glu
                  5
<210> 132
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<211> 10

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<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 132
Val Glu Ala Asn Tyr Ala Val Glu Gly Glu
                  5
<210> 133
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 133
Lys Thr Ile Asn Leu Glu Val Glu Pro Ser
          5
<210> 134
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<220>
<221> MOD_RES
<222> (5)
<223> Nle
<400> 134
Lys Thr Ile Asn Xaa Glu Val Glu Pro Ser
 1
                 5
<210> 135
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<221> MOD_RES
<222> (5)
<223> Nle
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 135
Lys Thr Ile Asn Xaa Glu Val Asp Pro Ser
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١

1 10 <210> 136 <211> 10 <212> PRT <213> Artificial Sequence <220> <221> MOD_RES <222> (5) <223> Nle <220> <223> Description of Artificial Sequence: synthetic peptide sequence <400> 136 Lys Thr Ile Asn Xaa Asp Val Asp Pro Ser -5 <210> 137 <211> 10 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: synthetic peptide sequence <400> 137 Lys Thr Ile Ser Leu Asp Val Glu Pro Ser 5 <210> 138 <211> 10 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: synthetic peptide sequence <400> 138 Lys Thr Ile Ser Leu Asp Val Asp Pro Ser 5 <210> 139 <211> 4 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: synthetic peptide sequence <400> 139

Lys Met Asp Ala

1

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<210> 140
<211> 4
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 140
Ser Tyr Glu Val
 1
<210> 141
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 141
Ser Glu Val Ser Tyr Glu Val Glu Phe Arg
              5
<210> 142
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 142
Asn Leu Asp Ala
 1
<210> 143
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 143
Ser Glu Val Ser Tyr Asp Ala Glu Phe Arg
<210> 144
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
```

peptide sequence

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<400> 144
Ser Glu Val Ser Tyr Glu Ala Glu Phe Arg
<210> 145
<211> 25
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 145
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
Glu Val Ser Tyr Glu Val Glu Phe Arg
             20
<210> 146
<211> 20
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 146
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Ser Tyr Glu
Val Glu Phe Arg
<210> 147
<211> 15
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 147
Lys Thr Glu Glu Ile Ser Glu Val Ser Tyr Glu Val Glu Phe Arq
                  5
                                      10
<210> 148
<211> 1.0
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
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<400> 148
Thr Glu Val Ser Tyr Glu Val Glu Phe Arg
                 5
<210> 149
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 149
Ser Glu Val Asp Tyr Glu Val Glu Phe Arg
<210> 150
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 150
Thr Glu Val Asp Tyr Glu Val Glu Phe Arg
<210> 151
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 151
Thr Glu Ile Asp Tyr Glu Val Glu Phe Arg
 1
                 5
<210> 152
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 152
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg
                  5
<210> 153
<211> 10
```

```
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 153
Ser Glu Ile Asp Tyr Glu Val Glu Phe Arg
<210> 154
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (11)
<223> Xaa=tryptophan
<223> Description of Artificial Sequence: synthetic
     peptide sequence
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
<210> 155
<211> 18
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (16)
<223> Xaa=tryptophan
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 155
Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa
                                      10
Lys Lys
<210> 156
<211> 23
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (21)
<223> Xaa=tryptophan
<220>
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<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 156
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val
Glu Phe Arg Xaa Lys Lys
        20
<210> 157
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<220>
<221> SITE
<222> (26)
<223> Xaa=tryptophan
<400> 157
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
                                      10
Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
             20
<210> 158
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (11)
<223> Xaa=tryptophan
<223> Description of Artificial Sequence: synthetic
      peptide sequence
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
<210> 159
<211> 18
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<220>
<221> SITE
```

```
<222> (16)
<223> Xaa=tryptophan
<400> 159
Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg
Xaa Lys Lys
<210> 160
<211> 23
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (21)
<223> Xaa=tryptophan
<223> Description of Artificial Sequence: synthetic
     peptide
<400> 160
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr
                                      10
                                                           15
Glu Val Glu Phe Arg Xaa Lys Lys
                20
<210> 161
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (26)
<223> Xaa=tryptophan
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 161
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
                20
<210> 162
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
```

```
<222> (11)
 <223> Xaa=oregon green
 <223> Description of Artificial Sequence: synthetic
       peptide sequence
 <400> 162
 Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
 <210> 163
 <211> 18
 <212> PRT
 <213> Artificial Sequence
 <220>
 <221> SITE
 <222> (16)
 <223> Xaa=oregon green
 <223> Description of Artificial Sequence: synthetic
      peptide sequence
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                   5
                                       10
 Lys Lys
 <210> 164
 <211> 23
 <212> PRT
 <213> Artificial Sequence
 <220>
<221> SITE
 <222> (21)
 <223> Xaa=oregon green
 <220>
 <223> Description of Artificial Sequence: synthetic
       peptide sequence
 <400> 164
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 Val Glu Phe Arg Xaa Lys Lys
              20
 <210> 165
 <211> 28
 <212> PRT
 <213> Artificial Sequence
 <220>
 <221> SITE
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<222> (26)
<223> Xaa=oregon green
<223> Description of Artificial Sequence: synthetic peptide sequence
<400> 165
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
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Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
             20
<210> 166
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (11)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 166
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
  1
                  5
                                      10
<210> 167
<211> 18
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (16)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 167
Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg
Xaa Lys Lys
<210> 168
<211> 23
<212> PRT
<213> Artificial Sequence
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<220>

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<222> (21)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 168
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                  5
                                      10
Glu Val Glu Phe Arg Xaa Lys Lys
<210> 169
<211> 28
<212> PRT
<213> Artificial Sequence
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<222> (26)
<223> Xaa=oregon green
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 169
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Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
<210> 170
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 170
Ser Glu Val Asn Tyr Glu Val Glu Phe Arg
<210> 171
<211> 47
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      primer for site-directed mutagenesis of APP
<400> 171
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```
<210> 172
<211> 48
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
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<210> 173
<211> 47
<212> DNA
<213> Artificial Sequence
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      primer for site-directed mutagenesis of APP
<400> 173
gagatetetg aaagtagtta tgaagtagaa tteegacatg acteagg
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<210> 174
<211> 48
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      primer for site-directed mutagenesis of APP
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                                                                   48
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gagatetetg aaattagtta tgaagcagaa tteegacatg acteagg
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<210> 176
<211> 48
<212> DNA
<213> Artificial Sequence
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      primer for site-directed mutagenesis of APP
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<210> 177
<211> 5
<212> PRT
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 Val Ser Tyr Glu Val
 <210> 178
 <211> 5
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      peptide sequence
 <400> 178
 Val Ser Tyr Asp Ala
 <210> 179
 <211> 5 .
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 <223> Description of Artificial Sequence: synthetic
      peptide sequence
 <400> 179
 Ile Ser Tyr Glu Val
  1
<210> 180
 <211> 5
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       peptide sequence
 <400> 180
Val Lys Met Asp Ala
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 <211> 47
 <212> DNA
 <213> Artificial Sequence
 <223> Description of Artificial Sequence: synthetic
       primer for generating mutant construct named
       MBPC125-SYEV
```

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<400> 181
gacatctctg aagtgagtta ttaggcagaa ttccgacatg actcagg
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<210> 182
<211> 48
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      primer for generating mutant construct named
      MBPC125-SYEV
<400> 182
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                                                                    48
<210> 183
<211> 6
<212> PRT
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     peptide sequence
<400> 183
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                  5
<210> 184
<211> 10
<212> PRT
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      peptide sequence
Val Glu Ala Asn Tyr Glu Val Glu Gly Glu
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<210> 185
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      peptide sequence
<400> 185
Val Glu Ala Asn Tyr Ala Val Glu Gly Glu
<210> 186
<211> 8
<212> PRT
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 186
Asp Tyr Lys Asp Asp Asp Lys
<210> 187
<211> 4
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: synthetic
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<400> 187
Ser Tyr Glu Ala
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Ser Tyr Ala Val
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      peptide sequence
<400> 189
Val Ser Tyr Glu Ala
 1
                  5
<210> 190
<211> 13
<212> PRT
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<223> Description of artificial sequence: synthetic peptide sequence
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<210> 191
<211> 23
<212> PRT
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<220>
<223> Description of artificial sequence: synthetic peptide sequence
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Val Glu Phe Arg Trp Lys Lys
            20
<210> 192
<211> 15
<212> PRT
<213> Artificial sequence
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<223> Description of artificial sequence: synthetic peptide sequence
<220>
<221> SITE
<222> (1)..(1)
<223> amino acid at position 1 is biotinylated
<220>
<221> SITE
<222> (14)..(14)
<223> cys at position 14 is derivatized with an oregon green
```

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<210> 193
<211> 22
<212> PRT
<213> Artificial sequence
<220>
<223> Description of artificial sequence: synthetic peptide sequence
<220>
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<222> (1)..(1)
<223> amino acid at position 1 is biotinylated
<220>
<221> SITE
<222> (21)..(21)
<223> cys at position 21 is derivatized with an oregon green
<400> 193
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu
Val Glu Phe Arg Lys Lys
<210> 194
<211> 6806
<212> DNA
<213> Artificial sequence
<220>
<223> Description of artificial sequence: synthetic DNA sequence
<400> 194
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                                                                     6600
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<210> 195
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<223> Description of artificial sequence: synthetic peptide sequence

<221> MOD RES

<222> (1)..(1)

<223> ACETYLATION (MCA)

<211> 13

<212> PRT

<213> Artificial sequence

<220>

<220>

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<221> SITE
<222> (11)..(11)
<223> 2,4-dinitrophenyl group after the Lys at position 11
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Ser Glu Val Asn Leu Asp Ala Glu Phe Arg Lys Arg Arg
<210> 196
<211> 12
<212> PRT
<213> Artificial sequence
<220>
<223> Description of artificial sequence: synthetic peptide sequence
<220>
<221> SITE
<222> (4)..(4)
<223> amino acid at position 4 has been derivatized with a statine
<400> 196
Ser Glu Val Asn Val Ala Glu Phe Arg Gly Gly Cys
<210> 197
<211> 10
<212> PRT
<213> synthetic peptide sequence
<220>
<221> SITE
<222>
      (4)..(4)
<223> amino acid at position 4 has been derivatized with a statine
<220>
```

<221> SITE

<222> (10)..(10)

<223> amino acid at position 10 has been derivatized with Bodipy FL

<400> 197

Ser Glu Val Asn Val Ala Glu Phe Arg Cys 1 5 10